REMARKS

Claims 17 and 19-24 are pending and stand ready for further action on the merits. Support for the amendment for claim 17 can be found in claim 18 and claim 2. Support for the amendment to claims 19-23 can be found in claims 3-7, respectively. Claim 24 has been amended so as not to depend from cancelled claim 18 and to improve clarity.

The specification has also been amended for clarity.

No new matter has been added by way of the above-amendment.

Issues under 35 U.S.C. 112, 2nd paragraph

Claims 1-16 and 18-24 are rejected under 35 U.S.C. 112, 2nd paragraph as being indefinite. Applicants respectfully traverse the rejection.

Applicants respectfully submit that the rejection of claims 1-16 is rendered moot in view of the cancellation of these claims.

The Examiner objects to claims 18-24 for indicating that the definition of certain substituents can be found in claims from which these particular claims depend from. In response, Applicants have amended these claims to either recite the definitions of the substituents therein or to be dependent from claims which recite the definitions.

In view of the above amendment and comments, Applicants respectfully submit that the claims particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Accordingly, withdrawal of the rejection is respectfully requested.

Issues under 35 U.S.C. 101

Claims 9-16 are rejected under 35 U.S.C. 101.

Applicants respectfully submit that this rejection is rendered moot in view of the cancellation of claims 9-16.

Issues under 35 U.S.C. 102(b)

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by JP 10-265454, US 5,892,099, and Kiriyama (British Journal of Pharmacology, 1997).

In view of the cancellation of claim 1, Applicants respectfully submit that this rejection is rendered moot.

Issues under 35 U.S.C. 103(a)

Claims 1-8 and 17-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isogaya US 5,508,303 (US '303). Applicants respectfully traverse the rejection.

The present inventors have surprisingly found that certain compounds which bind to the EP4 receptor subtype have hair generation or hair growth modulating actions.

Applicants respectfully submit that the present method is not made obvious by US '303, since US '303 describes that the compounds are IP agonists and do not have EP4 activity. For example, in US '303, beraprost is used in the working example. As shown in Table 3 of Kiriyama et al., a cited reference, it is clearly shown that beraprost does not bind to the EP4 receptor at all. Applicants note that some of the compounds included in Formula (I) as defined in present claim 17 overlap with the compounds disclosed in US '303. However, the present

invention is limited to the use of a prostaglandin EP4 receptor ligand. Accordingly, inventive claim 17 is limited to the use of compounds which act a prostaglandin EP4 receptor ligands. The compounds which do not act as prostaglandin EP4 ligands are excluded from claim 17, even if they are included in Formula (I). The compounds included in inventive Formula (I), which overlap with the compounds disclosed in US '303, do not act as prostaglandin EP4 receptor ligands. Therefore, the overlapping compounds are excluded from inventive claim 17 (even though they are included in inventive Formula (I)).

The Examiner appears to be finding that the present method is obvious over US '303, since the compounds of US '303 would inherently have prostaglandin EP4 receptor activity. Applicants respectfully submit that that which is inherent in the prior art, if not known at the time of the invention, cannot form a proper basis for rejecting claimed invention as obvious under section 103. In re Shetty, 195 USPQ 753 (CCPA 1977). Shetty claimed a composition of certain adamantane compounds and a method of using them to curb appetite in animals. The cited prior art taught similar compounds for use as anti-viral agents, with recommended dosages that corresponded to those claimed by appellant. The court did not affirm the PTO position of unpatentability regarding the method claims. Relying on prior art that taught anti-viral activity rather than appetite curbing activity, the PTO argued that administering the prior art compound in a dosage described in the art for anti-viral effectiveness, which corresponded to apellant's appetite curbing amount, would inherently achieve appetite curbing and thus render the claimed method obvious. Refusing to accept this position, the court responded that although Shetty's dosage amounts overlapped with the prior art, the court was not persuaded of the obviousness of appellant's method. Before Shetty had discovered an appetite curbing effect for the claimed

compounds, nothing in the art suggested using the similar prior art adamantanes to curb appetite much less in the claimed dosage amount. Obviousness cannot be predicated on what is unknown. "[Inherency] is quite immaterial if... one of ordinary skill in the art would not appreciate or recognize the inherent result." In re. Rijckaert, 28 USPQ2d 1955 (Fed. Cir. 1993).

In view of the foregoing, Applicants respectfully submit that the present method is not made obvious by US '303, and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above amendments and comments, Applicants respectfully submit that the claims are in condition for allowance. A notice to such effect is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Garth M. Dahlen, PhD. (43,575) at the telephone number of the undersigned below.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to February 13, 2003 in which to file a reply to the Office Action. The required fee of $930.00 is enclosed herewith.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____ #43575
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GMM/GMD/jmb
0760-0297P

Attachments: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph on page 2, lines 6-17 has been amended as follows:

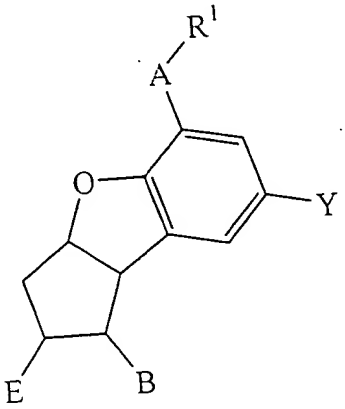
--[physiological] Physiological actions by PGE_2 are expressed by binding of PGE_2 to specific receptors. Further, the receptors to which PGE_2 bind may be classified into 4 receptor subtypes called EP1, EP2, EP3 and EP4 receptors (Coleman,R.A.et al., Pharmacol. Rev.,46,205-229(1994)). It is also known that each receptor subtype participates in different physiological action. For example, the febrile response by PGE_2 is caused by binding of PGE_2 to EP3 receptor (Ushikubi F., Nature, 395, 281-284 (1998)). It is known that compounds which specifically bind to EP4 receptor subtype are effective for prevention, therapy or amelioration of immune diseases, asthma, osteodystrophy, apoptosis of neurocytes, hepatopathy, nephritis, hypertension, myocardial ischemia, gastrointestinal disorder, shock and the like (Japanese Laid-open Patent Application (Kokai) No. 10-265454, WO98/55468). However, it is not known that these compounds have hair generation- or hair growth-modulating actions.--

IN THE CLAIMS:

Please amend the claims as follows:

17. (Amended) A method for modulating growth or generation of hair comprising administering a prostaglandin EP4 receptor ligand in an amount effective for modulating growth or generation of hair to human or an animal; wherein the said prostaglandin EP4 receptor ligand

is a 5,6,7-trinor-4,8-inter-m-phenylene PGI_2 derivative of the following Formula (I) or a pharmacologically acceptable salt thereof:

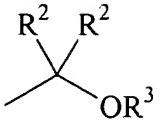


(I)

wherein

R^1 is

(i)



wherein R^2 is hydrogen, C_1-C_4 linear alkyl, C_3 or C_4 branched alkyl, trifluoromethyl, -C(=O)-R^4, or -C(=O)-O-R^4, wherein R^4 is C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl or substituted phenyl (wherein the substituent is at least one fluorine, chlorine, bromine, iodine, trifluoromethyl, C_1-C_4 alkyl, nitro, cyano, methoxy, phenyl, phenoxy, p-acetamidebenzamide, -CH=N-NH-C(=O)-NH_2, -NH-C(=O)-Ph, -NH-C(=O)-CH_3 or

-NH-C(=O)-NH_2), and the two R^2s may be the same or different; R^3 is hydrogen, C_1-C_4 alkyl, C_1-C_{12} acyl, C_7-C_{16} aroyl, C_7-C_{16} aralkyl, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl, allyl, tert-butyl or tert-butyldimethylsilyl,

(ii) -$COOR^5$

wherein R^5 is

(1) hydrogen or pharmacologically acceptable cation,

(2) C_1-C_{12} linear alkyl or C_3-C_{14} branched alkyl,

(3) -Z-R^6

wherein Z is a valence bond, or linear or branched alkylene represented by the formula C_tH_{2t} wherein t represents an integer of 1 to 6, R^6 is C_3-C_{12} cycloalkyl, or C_3-C_{12} cycloalkyl substituted with 1 to 4 R^7s wherein R^7 is hydrogen or C_1-C_5 alkyl,

(4) -$(CH_2CH_2O)_nCH_3$

wherein n represents an integer of 1 to 5,

(5) -Z-Ar

wherein Z is defined as the same as the above, Ar is phenyl, α-naphthyl, β-naphthyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, α-furyl, β-furyl, α-thienyl, β-thienyl or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above),

(6) -$C_tH_{2t}COOR^8$

wherein t is defined as the same as the above, R^8 is hydrogen or C_1-C_5 alkyl,

(7) -$C_tH_{2t}N(R^9)_2$

wherein t is defined as the same as above, R^9 is hydrogen or C_1-C_5 alkyl, and the two R^9s may be the same or different,

(8) $-CH(R^{10})-C(=O)-R^{11}$

wherein R^{10} is hydrogen or benzoyl, R^{11} is phenyl, p-bromophenyl, p-chlorophenyl, p-biphenyl, p-nitrophenyl, p-benzamidephenyl or 2-naphthyl,

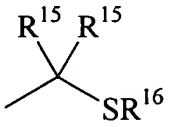
(9) $-C_pH_{2p}-W-R^{12}$

wherein p represents an integer of 1 to 5, W is -CH=CH-, $-CH=C(R^{13})-$ or $-C\equiv C-$ wherein R^{13} is C_1-C_{30} linear alkyl, C_3-C_{30} branched alkyl or C_7-C_{30} aralkyl, R^{12} is hydrogen, C_1-C_{30} linear alkyl, C_3-C_{30} branched alkyl or C_7-C_{30} aralkyl, or

(10) $-CH(CH_2OR^{14})_2$

wherein R^{14} is C_1-C_{30} alkyl or C_1-C_{30} acyl, and the two R^{14}s may be the same or different,

(iii)



wherein R^{15} represents is hydrogen, C_1-C_4 linear alkyl, C_3 or C_4 branched alkyl, trifluoromethyl, $-C(=O)-R^{17}$ or $-C(=O)-O-R^{17}$ wherein R^{17} is C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), and the two R^{15}s may be the same or different; R^{16} is hydrogen, C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, phenyl or

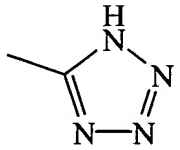
substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), or

-C(=O)-R^{18} wherein R^{18} represents C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above),

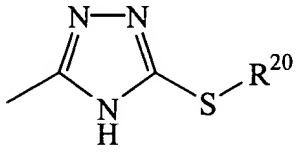
(iv) -CH_2-R^{19}

wherein R^{19} is

(1)

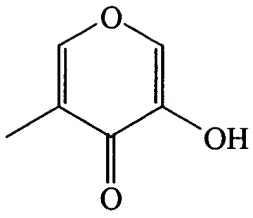


(2)

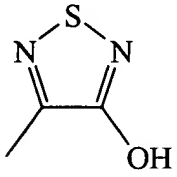


wherein R^{20} represents hydrogen, C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), or -C(=O)-R^{21} wherein R^{21} is C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl, or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above),

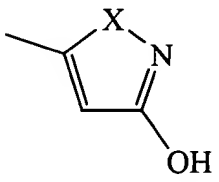
(3)



(4)



(5)



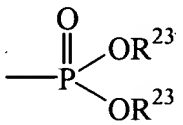
wherein X represents -O- or -S-, or

(6) azide,

(v) $-C(R^{22})_3$

wherein R^{22} represents hydrogen, fluorine, chlorine, bromine, iodine, cyano or C_1-C_4 alkyl, and all of the R^{22}s may be the same or different,

(vi)



wherein R^{23} represents hydrogen, C_1-C_4 alkyl, phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), -CH_2-OR^{24} (wherein R^{24} is C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl, or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), or pharmacologically acceptable cation, and the two R^{23}s may be the same or different,

(vii) $-N(R^{25})_2$

wherein R^{25} is hydrogen, C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_4-C_{13} cycloalkylalkyl, C_7-C_{12} aralkyl, $-C(=O)-R^{26}$, $-C(=O)-O-R^{26}$, $-SO_2-R^{26}$, phenyl or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), R^{26} is C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl or substituted phenyl (wherein the substituent is

the same as the substituent defined for the substituted phenyl mentioned above), the two R^{25}s may be the same or different (when one of the R^{25}s is $-SO_2-R^{26}$, the other R^{25} is not $-SO_2-R^{26}$),

(viii) $-(C(=O)CH_2)_k-H$

wherein k is an integer of 1 or 2, or

(ix) $-C(=O)-N(R^{27})_2$

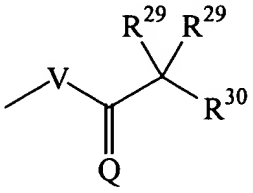
wherein R^{27} is hydrogen, C_1-C_{12} alkyl, C_3-C_{12} cycloalkyl, phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), C_4-C_{13} cycloalkylalkyl, C_7-C_{12} aralkyl, cyano or $-SO_2-R^{28}$ wherein R^{28} is C_1-C_{12} alkyl, C_3-C_{12} cycloalkyl, phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), C_4-C_{13} cycloalkylalkyl, or C_7-C_{12} aralkyl, and the two R^{27}s may be the same or different (when one of the R^{27}s is $-SO_2-R^{28}$, the other R^{27} is not

$-SO_2-R^{28}$);

Y is hydrogen, C_1-C_4 alkyl, fluorine, chlorine, bromine, formyl, methoxy or nitro;

B is

(i)



wherein V is

(1) $-CH_2CH_2-$,

(2) $-C\equiv C-$,

or

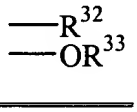
(3) $-CH=C(R^{31})-$

wherein R^{31} is hydrogen, C_1-C_5 alkyl, fluorine, chlorine, bromine or iodine,

Q is

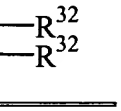
(1) =O

(2)



or

(3)



wherein R^{32} is hydrogen, C_1-C_4 linear alkyl, C_3 or C_4 branched alkyl, trifluoromethyl, -C(=O)-R^{34}, or -C(=O)-O-R^{34} wherein R^{34} represents C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_7-C_{12} aralkyl, phenyl or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above); R^{33} is hydrogen, C_1-C_4 alkyl, C_1-C_{12} acyl, C_7-C_{16} aroyl, C_7-C_{16} aralkyl, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl, allyl, tert-butyl or tert-butyldimethylsilyl, and the two R^{32}s may be the same or

different; R^{29} is hydrogen, fluorine, chlorine, bromine, iodine, cyano or C_1-C_4 alkyl, and the two R^{29}s may be the same or different;

R^{30} is

(1) -Z-R^{35}

wherein Z is defined as the same as the above, R^{35} is C_1-C_{12} linear alkyl, C_3-C_{14} branched alkyl, C_3-C_{12} cycloalkyl, C_4-C_{13} cycloalkylalkyl, C_3-C_{12} cycloalkyl substituted with 1 to 4 R^{36}s (wherein R^{36} is hydrogen or C_1-C_5 alkyl), C_4-C_{13} cycloalkylalkyl substituted with 1 to 3 R^{36}s (wherein R^{36} is defined as the same as the above), phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl mentioned above), α-naphthyl, β-naphthyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, α-furyl, β-furyl, α-thienyl or β-thienyl,

(2) -Z-O-R^{35}

wherein Z and R^{35} are defined as the same as the above,

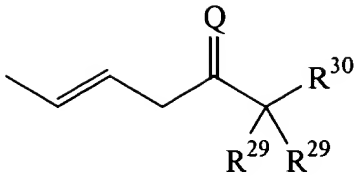
(3) -Z-CH=C(R^{35})$_2$

wherein Z and R^{35} are defined as the same as the above, and the two R^{35}s may be the same or different, or

(4) -Z-C≡C-R^{35}

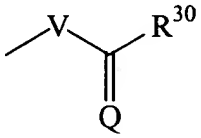
wherein Z and R^{35} are defined as the same as the above,

(ii)



wherein Q, R^{29} and R^{30} are defined as the same as the above, and the two R^{29}s may be the same or different, or

(iii)

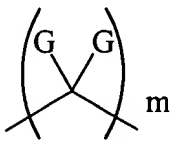


wherein V, Q and R^{30} are defined as the same as the above;

E represents hydrogen or $-OR^{33}$ wherein R^{33} is defined as the same as the above;

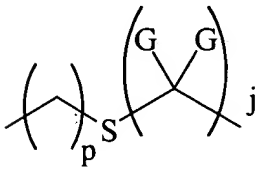
A is

(i)



wherein m represents an integer of 0 to 5, G represents hydrogen, fluorine, chlorine, bromine, iodine, trifluoromethyl, C_1-C_4 linear alkyl or C_3-C_6 branched alkyl, and all Gs may be the same or different,

(ii)



wherein j represents an integer of 1 to 4, p represents an integer of 0 or 1, G is defined as the same as the above, and all Gs may be the same or different,

(iii) -CH=CH-CH_2-,

(iv) -CH_2-CH=CH-,

(v) -CH_2-O-CH_2-,

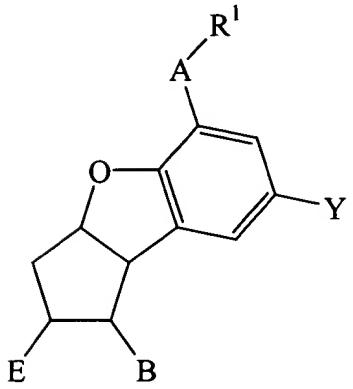
(vi) -O-CH_2-,

(vii) -C≡C-, or

(viii) -C=C- (trans).

19. (Amended) The method according to claim [18] 17, wherein the said 5,6,7-trinor-4,8-inter-m-phenylene PGI_2 derivative is represented by the following Formula (I) [(wherein the

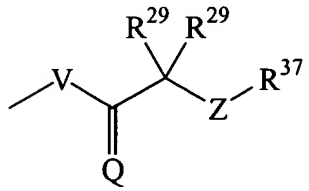
definitions of the substituents in Formula (I) are the same as the definitions of the respective substituents in Formula (I) in claim 3)] or a pharmacologically acceptable salt thereof:



(I)

wherein R^1, Y, E and A are defined in claim 17, B is

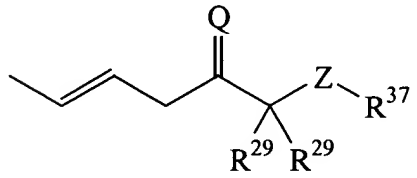
(i)



wherein V, Q, R^{29} and Z are defined in claim 17, the two R^{29}s may be the same or different, R^{37} is C_3-C_{12} cycloalkyl, C_4-C_{13} cycloalkylalkyl, C_3-C_{12} cycloalkyl substituted with 1 to 4 R^{38}s

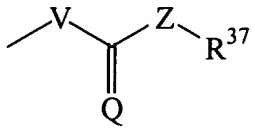
(wherein R^{38} is hydrogen or C_1-C_5 alkyl), C_4-C_{13} cycloalkylalkyl substituted with 1 to 3 R^{38}s (wherein R^{38} is defined as the same as the above), phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl in claim 17), α-naphthyl, β-naphthyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, α-furyl, β-furyl, α-thienyl or β-thienyl,

(ii)



wherein Q, R^{29}, Z and R^{37} are defined as the same as the above, and the two R^{29}s may be the same or different, or

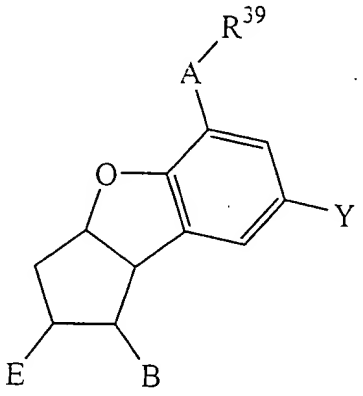
(iii)



wherein V, Q, Z and R^{37} are defined as the same as the above.

20. (Amended) The method according to claim [19] 17, wherein the said 5,6,7-trinor-4,8-inter-m-phenylene PGI_2 derivative is represented by the following Formula (II) [(wherein the

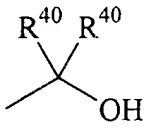
definitions of the substituents in Formula (II) are the same as the definitions of the respective substituents in Formula (II) in claim 4)] or a pharmacologically acceptable salt thereof:



(II)

wherein R^{39} is

(i)

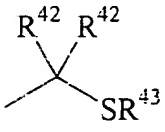


wherein R^{40} is hydrogen, C_1-C_4 linear alkyl or trifluoromethyl, the two R^{40} may be the same or different,

(ii) $-COOR^{41}$

wherein R^{41} is hydrogen, a pharmacologically acceptable cation or C_1-C_{12} linear alkyl,

(iii)

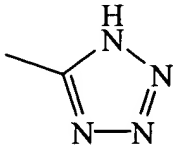


wherein R^{42} is hydrogen, C_1-C_4 linear alkyl or trifluoromethyl, the two R^{42}s may be the same or different, R^{43} is hydrogen, C_1-C_4 linear alkyl, phenyl, or -C(=O)-R^{44} wherein R^{44} represents C_1-C_4 linear alkyl,

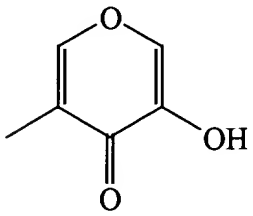
(iv) -CH_2-R^{45}

wherein R^{45} is

(1)

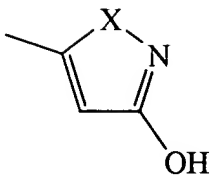


(2)



or

(3)

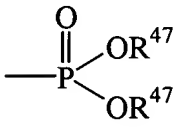


wherein X is defined in claim 17,

(v) $-C(R^{46})_3$

wherein R^{46} represents hydrogen, fluorine, cyano or C_1-C_4 alkyl, and all R^{46}s may be the same or different,

(vi)



wherein R^{47} represents hydrogen, C_1-C_4 alkyl, or a pharmacologically acceptable cation, and the two R^{47}s may be the same or different, or

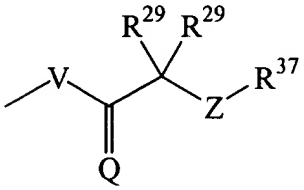
(vii) $-N(R^{48})_2$

wherein R^{48} is hydrogen, -C(=O)-R^{49} or -SO_2-R^{49} wherein R^{49} is C_1-C_4 linear alkyl or phenyl, and the two R^{48}s may be the same or different (when one of R^{48}s is -SO_2-R^{49}, the other R^{48} is not -SO_2-R^{49}),

Y is hydrogen, fluorine, chlorine or bromine,

B is

(i)



wherein V is

(1) -CH_2CH_2-,

(2) -C≡C-,

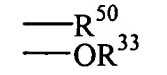
or

(3) -CH=CH-,

Q is

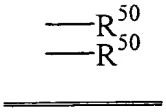
(1) =O,

(2)



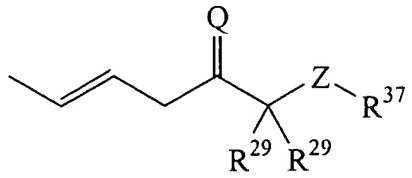
or

(3)



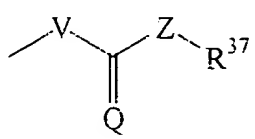
wherein R^{50} is hydrogen, C_1-C_4 linear alkyl, C_3 or C_4 branched alkyl, or trifluoromethyl, R^{33} is defined in claim 17, the two R^{50}s may be the same or different, R^{29} is defined in claim 17, and the two R^{29}s may be the same or different, Z is defined in claim 17, and R^{37} is C_3-C_{12} cycloalkyl, C_4-C_{13} cycloalkylalkyl, C_3-C_{12} cycloalkyl substituted with 1 to 4 R^{38}s (wherein R^{38} is hydrogen or C_1-C_5 alkyl), C_4-C_{13} cycloalkylalkyl substituted with 1 to 3 R^{38}s (wherein R^{38} is defined as the same as the above), phenyl, substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl in claim 17), α-naphthyl, β-naphthyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, α-furyl, β-furyl, α-thienyl or β-thienyl,

(ii)



wherein Q, R^{29}, Z and R^{37} are defined as the same as the above, and the two R^{29}s may be the same or different, or

(iii)

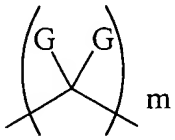


wherein V, Q, Z and R^{37} are defined as the same as the above,

E represents the following in the definition of claim 17,

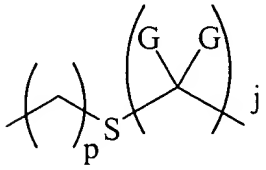
A is

(i)



wherein m represents an integer of 0 to 3, G is hydrogen, fluorine, chlorine, bromine, iodine, trifluoromethyl or C_1-C_4 linear alkyl, and all Gs may be the same or different,

(ii)



wherein j represents an integer of 1 or 2, p represents the following in the definition of claim 17, G is defined as the same as the above, and all Gs may be the same or different,

(iii) $-CH=CH-CH_2-$,

(iv) $-CH_2-CH=CH-$,

(v) $-CH_2-O-CH_2-$,

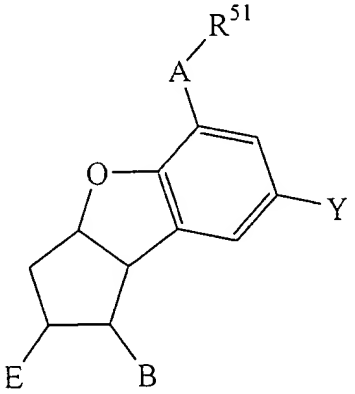
(vi) $-O-CH_2-$,

(vii) $-C\equiv C-$

or

(viii) -C=C- (trans).

21. (Amended) The method according to claim [20] 17, wherein the said 5,6,7-trinor-4,8-inter-m-phenylene PGI_2 derivative is represented by the following Formula (III) [(wherein the definitions of the substituents in Formula (III) are the same as the definitions of the respective substituents in Formula (III) in claim 5)] or a pharmacologically acceptable salt thereof:



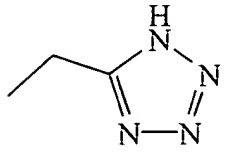
(III)

wherein R^{51} is

(i) $-COOR^{52}$

wherein R^{52} is hydrogen, a pharmacologically acceptable cation or methyl, or

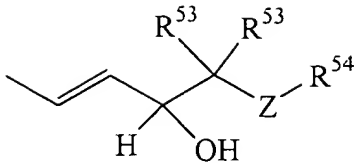
(ii)



wherein Y is hydrogen or fluorine.

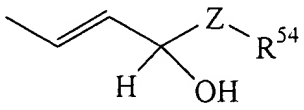
B is

(i)



wherein R^{53} is hydrogen, fluorine or C_1-C_4 alkyl, the two R^{53}s may be the same or different, Z represents the following in the definition of claim 17, R^{54} is C_5-C_7 cycloalkyl, phenyl, or substituted phenyl (wherein the substituent is the same as the substituent defined for the substituted phenyl in claim 17), or

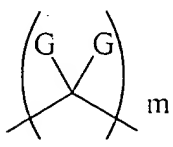
(ii)



wherein Z and R^{54} are defined as the same as the above,

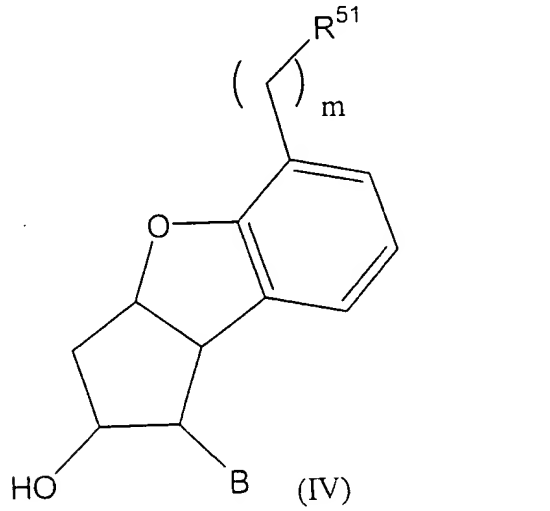
E is hydrogen or -OH,

A is



wherein m represents an integer of 0 to 2, G represents hydrogen or fluorine, and all Gs may be the same or different.

22. (Amended) The method according to claim [21] 17, wherein the said 5,6,7-trinor-4,8-inter-m-phenylene PGI_2 derivative is represented by the following Formula (IV) [(wherein the definitions of the substituents in Formula (IV) are the same as the definitions of the respective substituents in Formula (IV) in claim 6)] or a pharmacologically acceptable salt thereof:



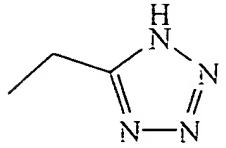
(IV)

wherein R^{51} is

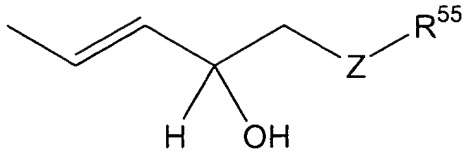
(i) $-COOR^{52}$

wherein R^{52} is hydrogen, a pharmacologically acceptable cation or methyl, or

(ii)

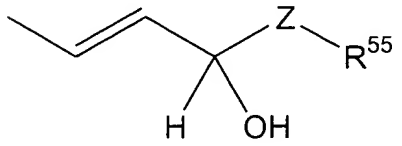


B is



(i)

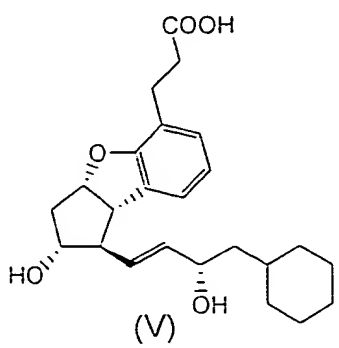
wherein Z represents the following in the definition of claim 17, R^{55} is C_5-C_7 cycloalkyl or phenyl, or



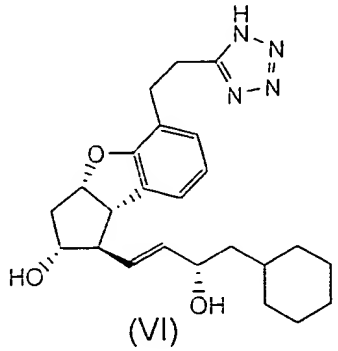
(ii)

wherein Z and R^{55} are defined as the same as the above, m represents an integer of 0 to 2.

23. (Amended) The method according to claim [22] 17, wherein the said 5,6,7-trinor-4,8-inter-m-phenylene PGI_2 derivative is represented by the [said] following Formula (V) or (VI):



(V)



(VI)

24. (Amended) The method according to any one of claims 17 and 19 to 23, wherein the said [agent] method for modulating growth or generation of hair is [an agent] a method for promoting growth or generation of hair.

Claims 1-16 and 18 have been cancelled.